

1. A method for generating a mutagenized polynucleotide comprising:

a) annealing a poly-binding nucleic acid strand to two or more mono-binding nucleic acid strands to generate an annealed heteromeric complex of nucleic acid strands;

b) subjecting unhybridized single-stranded ends of the annealed mono-binding nucleic acid strands in the heteromeric complex to an exonuclease treatment that degrades said unhybridized ends; and

c) subjecting the annealed heteromeric complex to polymerase-based extension.

2. The method of claim 1, further comprising d) subjecting the annealed nucleic acid strands to a ligase treatment.

3. The method of claim 1, further comprising:

e) separating the poly-binding nucleic acid strand from the ligated mono-binding nucleic acid strands.

4. The method of claim 1, further comprising:

f) generating a nucleic acid strand that is complementary to the ligated mono-binding nucleic acid strand, whereby the resultant product is comprised of a double stranded mutagenized progeny polynucleotide.

5. The method of claim 1, wherein the polynucleotide is a gene or gene pathway.

6. The method of claim 1, wherein the poly-binding nucleic acid strand and the two or more mono-binding nucleic acid strands are each derived from a different parent template.

7. The method of claim 1, wherein the ligase treatment is by subjection to T4 DNA Ligase.

8. The method of claim 1, wherein the method is performed in vitro.

9. The method of claim 1, wherein the method is performed in vivo.

10. The method of claim 1, wherein the exonuclease treatment comprises subjection to a 3' exonuclease treatment, subjection to a 5' exonuclease treatment, treatment with Mung Bean Nuclease, treatment with S1 Nuclease red alpha exonuclease, venom phosphodiesterase, or treatment with E.coli DNA Polymerase.

11. The method of claim 1, wherein annealed complex comprises about 10, 100, 1000, 10000, 100,000 or 1,000,000 bases.

12. The method of claim 1, wherein the mono-binding strands and/or the poly-binding strands are generated from a template progenitor molecule by synthesis, fragmentation, isolation or denaturation.

13. The method of claim 1, wherein the mono-binding strands and/or the poly-binding strands are derived from a library of clones generated from nucleic acid from a mixed population of organisms.

14. The method of claim 13, wherein the organisms are microorganisms.

15. The method of claim 14, wherein the microorganisms are a mixed population of microorganisms.

16. The method of claim 14, wherein the microorganisms are uncultured microorganisms.

17. The method of claim 14, wherein the microorganisms are from an environmental sample.